REMARKS

Reconsideration and allowance are respectfully requested.

Claims 1-23 and 27-41 are pending. Non-elected claims 24-32 were withdrawn from consideration by the Examiner. Applicants cancel non-elected claims 24-26 without prejudice to future prosecution of that subject matter. Upon allowance of an elected product claim, rejoinder of non-elected method claims 27-32 is requested.

Enclosed are Form PTO-1449 and documents listed therein, which are submitted for consideration by the Examiner. The fee required by 37 CFR § 1.17(p) is attached in lieu of certification. As provided by 37 CFR §§ 1.97(g) and (h), no representation is being made that a search has been conducted or that this statement encompasses all possible material information. Furthermore, no inference should be made that this information or the cited references are prior art merely because they have been submitted for consideration. In accordance with 37 CFR § 1.97(c), consideration of the foregoing and enclosed documents, as well as the return of a copy of the Form PTO-1449 with the Examiner's initials per M.P.E.P. § 609, are earnestly solicited.

Specification/Claim Objections

The specification was objected to as allegedly informal. Thus, the formatting of the abstract is corrected as required by the Examiner.

Claims 1 and 4-5 were objected as allegedly encompassing non-elected subject matter, but the latter needs to be maintained to allow later withdrawal of the requirement or rejoinder upon an indication that there is patentable subject matter.

Withdrawal of the objections is requested.

35 U.S.C. 112 – Definiteness

Claims 1-23 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Applicant traverses.

The claims are amended to clarify what is meant by a "variant" sequence. For example, claim 1, part (c) now defines the variant sequence by percent identity to the

polypeptide of SEQ ID NO:2. The phrase "equivalent to" is replace with --corresponding to--. That is, in the sequences of claim 1, parts (b) and (c), the mutations exist at the amino acid residues corresponding to at least one of W433, E432 and M439 of SEQ ID NO:2. The skilled person would routinely be able to identify the appropriate amino acid residues; an illustration of how this may be done is in Fig. 1 of Applicant's specification.

Applicant requests withdrawal of the Section 112, second paragraph, rejection because the pending claims are clear and definite.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-23 were rejected under Section 112, first paragraph, because it was alleged that the specification "does not reasonably provide enablement for any carbohydrate processing or degrading or synthesizing enzyme or any variant of SEQ ID NO:2 or any mutation in SEQ ID NO:2 at any position or any mutation at any position equivalent to M439 or any polypeptide having one or more position substituted by any amino acid." Applicant traverses.

Claim 1 as amended refers to polypeptides having a specific enzymatic activity: carbohydrate processing. Three particular classes of polypeptide are defined in claim 1. Firstly, part (a) specifies the amino acid sequence of SEQ ID NO:2 comprising one of three specific mutations. The effects of these three mutations are demonstrated in Applicant's specification.

Secondly, claim 1, part (b) refers to family 1 glycosyl hydrolases which comprise a mutation at an amino acid residue corresponding to at least one of three specific amino acidresidues in SEQ ID NO:2. A polypeptide according to claim 1, part (b) is

therefore defined in a number of ways. Firstly, it is defined in functional terms as having carbohydrate processing enzymatic activity. Secondly, it is defined as being a family 1 glycosyl hydrolase.

Glycosyl hydrolases are a specific group of carbohydrate processing enzymes which hydrolyze the glycoside bond between two or more carbohydrates or between a carbohydrate and a non-carbohydrate moiety. The glycosyl hydrolases are classified into families based on amino acid sequence similarities. Enclosed is a review which discusses the family classification of carbohydrate processing enzymes and in particular glycoside hydrolases (Henrissat & Coutinho, in *Carbohydrate Bioengineering*, RSC Publishing, pp. 171-177, 2002). As explained in that document, this classification was introduced in 1991, and was rapidly and almost universally adopted by those skilled in the art. As explained in the first full paragraph on page 172 of Henrissat & Coutinho, this classification is based on the amino acid sequence similarities within the catalytic domains of these enzymes. Because there is a direct relationship between sequence and folding similarities, this classification into families reflects the structural features of these enzymes and can be used to derive mechanistic information. A number of crucial features of enzyme action, catalysis, evolution and 3-D structure are revealed by the sequence classification in a powerful predictive manner.

Thus, the family 1 glycosyl hydrolases of claim 1, part (b) are a tightly defined group of enzymes and may be easily identified by the skilled reader. By specifying a family 1 glycosyl hydrolase, not only is the function of the enzyme as glycosyl hydrolase defined, the enzyme is also defined by sequence characteristics. Claim 1, part (b) thus clearly defines a group of enzymes in terms of their structure and function. A person skilled in the art would be well aware of the family classification for carbohydrate processing enzymes and could easily determine whether an enzyme was, or was not, a family 1 glycosyl hydrolase.

Furthermore, in view of the sequence and functional similarities within the family 1 group of glycosyl hydrolases, the skilled person would reasonably expect that mutations at positions corresponding to amino acid residues of SEQ ID NO:2 would have a similar effect on other family 1 glycosyl hydrolases to those exemplified in Applicant's

specification with respect to SEQ ID NO:2. Based on the well known characteristics of this group of enzymes, as discussed in Henrissat & Coutinho, the skilled person would be aware of regions of the protein structure which may be modified without affecting carbohydrate processing activities and it would be reasonable to predict the effect of mutations on such enzymes based on the data in the present application with respect to SEQ ID NO:2. The scope of the claims is therefore believed to be reasonable in view of the teachings and supporting working examples present in Applicant's specification.

Finally, claim 1, part (c) defines variants of SEQ ID NO:2 in terms of amino acid sequence identity to SEQ ID NO:2. As explained on pages 11-12 of the specification, such a variant may have a specified level of identity to SEQ ID NO:2 over the entire length of the sequence. Alternatively, the variant may have a specified level of identity to the particular region of SEQ ID NO:2 from residue 425 to 450. Claim 1, part (c) thus defines variants of SEQ ID NO:2 both in terms of their function (i.e., the activity of a carbohydrate processing enzyme) and their amino acid sequence (i.e., percent identity and specific mutations). New claims 33-38 define increasing levels of amino acid sequence identity to SEQ ID NO:2 for a variant sequence of claim 1, part (c).

Enclosed are partial extracts from two books relating to bioinformatics (*Bioinformatics*, Lesk, Oxford University Press, pp. 184-187, 2002; and *Bioinformatics: Genes, Proteins & Computers*, Orengo et al., Garland Science/BIOS Scientific Publishers, Chapter 3, pp. 29-46, 2003). These documents discuss the use of amino acid sequence identity to identify homologs of existing polypeptides. Lesk teaches at page 185:

> Many 'rules of thumb' are expressed in terms of percent identical residues in the optimal alignment. If two proteins have over 45% identical residues in their optimal alignment, the proteins will have very similar structures, and are very likely to have a common or at least a similar function. If they have over 25% identical residues, they are likely to have a similar general folding pattern. On the other hand, observations of a lower degree of sequence similarity cannot rule out homology. R.F. Doolittle defined the region of 18 to 25% sequence identity as the 'twilight zone' in which the suggestion of homology is tantalizing, but dangerous.

This general teaching is repeated by Orengo et al. at page 30:

> Sander and Schneider have shown empirically that sequences of 100 residues or more, sharing at least 35% identical residues, are definitely

> homologs; a result confirmed recently by Rost with a much largest dataset (see Figure 3.1).

Orengo et al. further teach:

> Pair-wise sequence alignment methods are generally used to detect close homologs (≥ 35% identity) and even to reveal evolutionary relationships in what Doolittle has referred to as the twilight zone of sequence similarity, i.e. down to as low as 25% identity.

It is therefore reasonable for a person skilled in the art to believe that the variants of claim 1, part (c) are homologs of the polypeptide of SEQ ID NO:2. An amino acid sequence at least 30% identical to SEQ ID NO:2, or more particularly to the region from residue 425 to 450, combined with the functional requirement that the variant has carbohydrate processing enzymatic activity, establishes that the variant is a homolog of the polypeptide comprising SEQ ID NO:2 and that mutations at amino acid residues corresponding to those identified in SEQ ID NO:2 would reasonably be expected to have the same or similar effects.

Polypeptides falling within the scope of the claims are therefore well defined by the claims. These polypeptides are defined with reference to their activity and to their structural characteristics (i.e., amino acid sequence). Based on Applicant's teachings in his specification, it can be reasonably believed that the mutations specified in the claims will lead to similar effects in those polypeptides to those demonstrated in the specification with respect to SEQ ID NO:2.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

35 U.S.C. 102 – Novelty

Claims 1-5 and 18-19 were rejected under Section 102(a) as allegedly anticipated by Corbett et al. (FEBS Lett. 509:355-360, 2001). Applicant traverses.

Enclosed is a Declaration by the inventor. It confirms that the inventor was the primary author of Corbett et al. The cited document was published less than one year

prior to the filing of the priority Application No. 60/416,263. Therefore, the Corbett et al. document is not prior art disclosure of another.

Withdrawal of the Section 102 rejection is requested.

35 U.S.C. 103 – Nonobviousness

Claims 16-17 and 20-23 were rejected under Section 103(a) as allegedly unpatentable over Corbett et al. (FEBS Lett. 509:355-360, 2001) in view of Withers et al. (US 2003/0138880 A1). Applicant traverses for the reason below.

Claims 6-15 were rejected under Section 103(a) as allegedly unpatentable over Corbett et al. (FEBS Lett. 509:355-360, 2001) in view of DeSantis et al. (Biochemistry 37:5968-5973, 1998). Applicant traverses for the reason below.

As discussed above, Corbett et al. is not a prior art disclosure of another. Absent the disclosure of Corbett et al., Withers et al. and DeSantis et al. fail to provide sufficient teaching or suggestion to render obvious the claimed invention.

Withdrawal of the Section 103 rejections is requested.

Conclusion

Having fully responded to all of the pending objections and rejections contained in this Office Action, Applicant submits that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100